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High prevalence of erectile dysfunction in diabetes:

A systematic review and meta-analysis of 145 studies

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ABSTRACT (250/250)

Objective: Erectile dysfunction (ED) may be common among people with diabetes, but its prevalence and odds versus controls is still unknown. We therefore aimed to assess the prevalence of ED in diabetes via a meta-analysis.

Research design and methods: We searched major databases from inception to11/2016 for studies reporting ED in people with diabetes (type I (T1DM), type II (T2DM) and both). We conducted a meta-analysis of the prevalence (and 95% confidence-intervals (CIs)) of ED in diabetes and where possible compared this versus healthy controls (HCs), calculating the relative odds ratios (ORs)and 95% CIs. A random effect model was applied.

Results: Out of 3747 initial hits, 145 studies were included representing 88,577 male participants with diabetes (55.8±7.9 years, T1DM=5,604, T2DM=44,488, both=20.061, not reported=18,424). The overall prevalence of ED in diabetes was 52.5% (95%CI: 48.8-56.2 after adjusting for publication bias). The prevalence of ED was 37.5%, 66.3% and 57.7% in T1DM, T2DM and both respectively (p for interaction<0.0001). The prevalence of ED was highest in studies the Sexual Health Inventory for Men (82.2%, studies =17, p for interaction<0.0001). Only higher percentage of people with hypertension moderated our results (beta=0.03; 95%CI: 0.008-0.004; p=0.003; R^2=0.00). Compared to HCs (n=5,385) people with diabetes (n=863) were at increased odds of having ED (OR=3.62; 95%CI: 2.53-5.16, p<0.0001; I^2=67%, k=8).

Conclusions: ED is common in diabetes, affecting more than half of people with diabetes and is approximately 3.5 times more likely versus controls. Our findings screening and offering appropriate interventions for people with ED may be useful.

INTRODUCTION

Diabetes mellitus (DM) is defined as a chronic metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both and leading to hyperglycemia or raised blood sugar.(1) The WHO Global Report on Diabetes states that the number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014 and that the global prevalence among adults has risen from 4.7% to 8.5% in the same years.(2) The main and most considered complications of diabetes weigh on the heart, blood vessels, eyes, kidneys, nerves.(3) In addition to the traditional complications, diabetes has been associated with increased rates of specific cancers (pancreatic, hepatobiliary, breast, endometrial and colorectal cancer)(4) and physical and cognitive disability, and finally to depression.(5; 6)

Increasing attention is turning to erectile dysfunction (ED) in diabetic patients due to its multifactorial pathophysiology and the concurrence of the same components as vasculopathy, neuropathy and depression. (7) ED is defined as the inability to achieve and/or maintain an erection sufficient to permit satisfactory sexual intercourse.(7) Although ED is considered an age-related disease affecting 20% of men above 40 years, also before it can be present especially when coexist risk factors as diabetes, metabolic syndrome or cardiovascular diseases, although it is probably underestimated in younger people.(8) DM is considered the main risk factor for the development of ED and since the 70s the association between DM and the development of erectile dysfunction has been documented both in animal models and humans.(9; 10)

Although previous studies have suggested that ED is more prevalent in people with diabetes compared to healthy subjects(11), the exact prevalence of this condition is still unclear in people with DM. A number of narrative reviews(12-15) have considered the prevalence of ED in DM and the majority agree that the incidence of ED in men with diabetes is two/three-fold higher than in the general

population. It is estimated that ED affects up to 75% of all diabetic men, it is age correlated and occurs at a younger age in patients with DM.

Even if all these works advanced our knowledge regarding this issue, the exact prevalence of ED in DM is still not known, but it could be of importance since ED, for example, is associated with higher cardiovascular risk in people with DM. (16-20). Moreover, no meta-analysis has compared the odds of ED versus controls and meta-regression of the factors which may influence ED among people with diabetes are not known.

Given this background, the aim of this study was to assess the prevalence of ED in diabetes, using a meta-analytic approach.

METHODS

This systematic review adhered to the PRISMA(21) and MOOSE(22) statements and followed an *a priori* defined, but unpublished protocol.

Data sources and literature search strategy

Two investigators (DP and YK) independently conducted a literature search using PubMed, EMBASE, SCOPUS, from database inception until 01st November, 2016. All the studies reporting the prevalence of ED in diabetes were considered. In PubMed, the following search strategy was (diabetes*) AND (erectile dysfunction OR erectile function OR sexual dysfunction OR sexual function) AND (prevalence or odds or risk). An identical search was conducted in the other databases. Conference abstracts and reference lists of included articles were hand-searched to identify and potential additional relevant articles. Any inconsistencies were resolved by consensus with a third author (BS).

Study selection

Studies were included in meta-analysis if: i) reported the prevalence of ED; ii) used a validated instrument for the diagnosis of ED such as the international index of erectile function (IIEF)(23) or the Sexual Health Inventory for Men (24)(SHIM); iii) included people with a validated diagnosis of diabetes (e.g. with the criteria suggested by the American Diabetes Association)(1) ; iv) included male participants.

Studies were excluded if: i) were not conducted in humans; ii) included participants with ED, but not diabetes; iii) included participants having all both diabetes and ED (i.e. prevalence=100% and a biased sample); iv) included only females.

Data extraction

Two independent investigators (DP and YK) extracted key data from the included articles in a standardized Excel sheet and a third independent investigator (NV) validated data extraction. For each article, we extracted data regarding authors, year of publication, country, setting, demographics (i.e. sample size, mean age), type of diabetes, diagnostic criteria used for ED, duration of diabetes, percentage of participants having the most common complications of diabetes (neuropathy, retinopathy, cardiovascular disease, kidney failure) and some known risk factors for ED (smoking, obesity, hypertension).

When some information was missing, first and/or corresponding authors of the original article were contacted at least two times in a month to obtain the variables of interest. For 23 eligible papers, we were unable to acquire the full texts and the authors did not respond to our requests. However, these conference abstracts contained sufficient data for meta-analysis.

Outcomes

The main outcome of interest was the prevalence of ED in people with diabetes reported in the original paper both as percentage or as number of ED/number of people with diabetes. Where available, also data regarding the prevalence of ED in healthy controls with no diabetes was extracted.

Assessment of study quality

Two authors (NV, DP) assessed the quality of the studies included taking in account these factors: i) clear diagnostic criteria for diabetes; ii) clear diagnostic criteria for ED; iii) reporting the prevalence of at least one diabetic complication; iv) reporting data on the duration of diabetes.

Data synthesis and statistical analysis

All analyses were performed using Comprehensive Meta-Analysis (CMA) 3 (http://www.meta-analysis.com).

In the primary analysis, we calculated the prevalence of ED in diabetes with its 95% confidence intervals (CIs) applying a random-effect model due to an anticipated heterogeneity.(25) The prevalence was reported as percentage. In secondary analysis, the prevalence of ED in diabetic vs. controls was compared using odds ratios (ORs) with their 95%Cis.

Heterogeneity across studies was assessed by the I^2 metric and Cochran's Q chi-square statistics with a value$\geq$50% for the first and a p-value<0.05 indicating the presence of a significant heterogeneity.(26) In case of high heterogeneity, sensitivity and meta-regression analyses were run in order to identify possible moderators of this heterogeneity. In sensitivity analyses, we stratified our results by continent (Africa, Asia, Europe, North and South America, Oceania, multi-continent), type of diabetes (type 1, 2, studies including both forms, or not declared), setting (community, outpatients, not declared), type of article (original article or conference abstract), diagnostic tools for the presence of ED (IIEF-5, SHIM or other tools) and mean age (divided in 18-60 years and $\geq$ 60 years or not declared). In meta-regression analysis, we analyzed some potential moderators as continuous variables in the sample as whole, namely: duration of diabetes (years), percentage of people with neuropathy, retinopathy, cardiovascular disease, kidney failure, hypertension; mean body mass index; percentage of actual smokers.

Publication bias was assessed by visually inspecting funnel plots and using the Egger bias test.(27) Then, to account for publication bias, we used the trim-and-fill method, based on the assumption that the effect sizes of all the studies are normally distributed around the center of a funnel plot; in the event of asymmetries, it adjusts for the potential effect of unpublished (imputed) studies.(28)

Finally, we calculated the fail-safe number of negative studies that would be required to nullify each of our comparative analyses (i.e., result in $p>0.05$).

For all analyses, $p<.05$ was considered statistically significant.

RESULTS

Search results

The search yielded 3,747 non-duplicated articles. After excluding 3,441 articles based on title/abstract review, 306 articles were retrieved for full text review and 145 studies were finally included (**Figure 1**).

Study and participants' characteristics

Full descriptive details of the included studies are reported in **Supplementary Table 1**.

Altogether, this meta-analysis included 145 studies (for the references see **Supplementary Table 2**) and 88,577 male participants with diabetes aged a mean of 55.8±7.9 years (range:23.4-71.7 years).
The majority of the studies was made in Asia (61 studies, =41.8%), followed by Europe (48, =32.9%), North America (17, =11.6%) and Africa (15, =10.3%). All studies, except 14, were made among outpatients. Finally, most studies included people having a diagnosis of type 2 diabetes (70 studies for a total of 44,488 participants), followed by studies that did not declare which type of diabetes was included (45 studies, n=18,424), both type 1 and 2 (18 studies, n=20,061) and only type 1 (12 studies, n=5,604). The presence of ED was diagnosed mainly through the IIEF-5 (n=90 studies).
The most common source of bias was the absence of data regarding diabetic complications, since these information were present in only 32 (=22.1%) of the studies included.

Prevalence of ED in diabetes

As shown in **Table 1**, the overall prevalence of ED in diabetes was 59.1% (95%CI: 55.5-62.7). This finding was characterized by a high heterogeneity (I^2=99%) and by a publication bias (Egger's test=3.71±1.32, p=0.006). After conducting the trim and fill analysis, 20 studies missing on the left were adjusted and the adjusted prevalence of ED in diabetes was 52.5% (95%CI: 48.8-56.2) (**Table 1**).

Factors affecting ED prevalence

As shown in **Table 1**, the prevalence of ED was significantly higher (between groups p-value<0.0001) in the studies made in South America (prevalence=74.6%; 1 study), Oceania (prevalence=74.4%; 1 study) and Africa (prevalence=71.3%; 15 studies) and lower among North Americans (prevalence=34.5%; 17 studies).

The prevalence of ED resulted significantly higher in patients with type 2 diabetes (prevalence=66.3%; 70 studies) compared to type 1 diabetes (prevalence=37.5%; 12 studies) (p for interaction<0.0001). Moreover, the prevalence of ED was significant higher in the studies using the SHIM for assessing ED (prevalence=82.2%; 17 studies) and those having a mean age over 60 years (prevalence=66.7%; 23 studies) (**Table 1).** On the contrary, the setting in which the study was performed (p for interaction=0.37) and the type of article (p for interaction=0.79) resulted no significant moderators of our findings.

Meta-regression analysis

Since our main outcome was characterized by a high heterogeneity (I^2=99%) and the stratification shown in Table 1 was not able to explain any heterogeneity, we assessed if other factors could explain this heterogeneity. As shown in **Table 2** among some potential possible moderators (including the most common chronic complication of diabetes, duration of diabetes and risk factors for ED such as smoking) only higher percentage of people with hypertension moderated our results (beta=0.03; 95%CI: 0.008-0.004; p=0.003) without, however, explaining any heterogeneity (R^2=0.00).

Comparison with the controls

Eight studies (29-36) reported the prevalence of ED in diabetic (n=863) versus healthy controls (n=5,385). As shown in **Figure 2**, the prevalence of ED in diabetic people vs. controls was almost doubled (51.6% vs. 25.5%), leading to an overall OR=3.62 (95%CI: 2.53-5.16, p<0.0001; I^2=67%). No

evidence of publication bias was present for this outcome (Egger's test=2.21±1.44, p=0.17) and the fail-safe number was 311.

DISCUSSION

To the best of our knowledge, this is the first meta-analysis to assess the prevalence of ED in diabetes mellitus synthesizing a large volume of international literature (including 145 studies and 88,577 male diabetic participants). We showed an overall prevalence of ED of 59.1% in diabetes patients (52.5% if adjusted for publication bias). This condition was significantly higher in people with type 2 diabetes compared to type 1 diabetes, and in older participants. Men with diabetes tend to develop erectile dysfunction 10 to 15 years earlier than men without diabetes.(37) In fact, ED is the third most frequent complication of diabetes that affects the quality of life and it is often indicative of underlying vasculopathy representing a predictor of more serious cardiovascular disorders.(38) As the prevalence of diabetes rises inexorably in high, middle, and low income countries alike, our work aimed to give an overall estimate of ED in diabetes.

One of our main results is that the prevalence of ED in diabetes patients is 3 folds higher than controls with an overall OR=3.62 (95%CI: 2.53-5.16, p<0.0001; I^2=67%) and more higher among patients with a mean age over 60 years. These findings are consistent with the Massachusetts Male Aging Study(39) in which diabetic men showed a threefold probability of having ED than men without diabetes and the age-adjusted risk of ED was doubled in diabetic men compared with those without diabetes.(40) Notably, the global ageing of the world population as well as the dramatical increasing prevalence of diabetes mellitus may explain the worldwide prevalence of ED, which has been estimated to 322 million cases by the year 2025.(41)

A comprehensive review including high-quality studies undertaken by Kamenov and colleagues(14) agreed with our findings that advanced age and type 2 diabetes are associated with an increased risk of ED. In addition, as shown in our analyses the prevalence of ED in type 2 diabetes patients is higher compared to type 1 diabetes. Indeed, many patients may already have ED at the diagnosis of type 2 diabetes. ED has been proven to be the first sign of diabetes, diagnosed later in 12–30 % of men.(42)

Recently, Corona et al., found in a sample of 499 men (mean age 58.8 ± 8.8 years) with new or recently diagnosed type 2 diabetes mellitus: mild ED in 19.4 %, mild-to-moderate in 15.4 %, moderate in 10.4 %, and severe in 21.6 % of patients. (43)

Several cross-sectional and longitudinal studies showed an association between ED and most of the classical cardiovascular risk factors, including smoking(44), diabetes(45), hypertension(46), hyperlipidemia(47), metabolic syndrome(48), as well as depression.(49) Surprisingly, in our meta-regression analysis, hypertension only was associated with the diabetes-related ED (p=0.003). However, in a large survey of 7689 patients with diabetes and/or hypertension, ED according to the IIEF-5 score was present in 67% of patients with hypertension alone, in 71% with diabetes alone, and increased to 77% of patients with both diseases.(46)

There is increasing evidence of a direct link between ED and cardiovascular diseases.(50) ED is a marker of early atherosclerosis and it is considered not only as a part of the quality of life but also as an independent predictor of cardiovascular events and all-cause mortality as well.(51) Several identified factors contribute to the complex pathogenesis of diabetes related ED including diabetic neuropathy, micro- and macro-vascular arterial disease (oxidative stress, endothelial dysfunction, dyslipidemia, arterial hypertension, etc.), hypogonadism, psychogenic components and drug side effects.(14; 52) The diagnostic process is based on the results of standardized questionnaires, vascular and neurological investigations. One of the most used and practical questionnaires that is administered is the International Index of Erectile Function (IIEF)-5, whom a score of 21 or less indicates the presence of ED.(53) However, depending on the age, duration and type of diabetes mellitus and the used diagnostic criteria epidemiological data about diabetes related ED vary significantly between different studies.(38) Our analysis show large differences in the reported prevalence of ED approximately from 35% to 80% among diabetic men which could be due to differences in methodology and population characteristics. Advancing age, duration of diabetes, poor

glycaemic control, hypertension, hyperlipidemia, sedentary lifestyle, smoking, and presence of other diabetic complications have been shown to be associated with diabetes related ED in cross-sectional studies.(38)

ED

Regarding sexual activity and the psychological impact of ED in patients with diabetes mellitus, significant and positive associations between depressive symptoms and ED have been found. In addition, ED strongly contributes to poorer quality of life in patients with diabetes mellitus. Therefore, early detection of ED is essential to improve the psychological health and patients' quality of life.

Whilst our data offers novel insight into the extent of ED among people with diabetes, some limitations need to be considered. One of them is the difficulty to provide the ED prevalence by categories because of incomplete data available in published studies. Secondly, most information refers to the total diabetic population and few studies have presented data separately for Type 1 and Type 2 diabetes patients. And thirdly, the analysis of the others risk factors contributing to the diabetes-related ED was limited because of the small number of primary studies that provide complete clinical and biological features of the patients.

In conclusion, our study provides worldwide data on the prevalence of and risks factors for ED in diabetes. The relationship of ED with certain risk factors, such as age or cardiovascular risk factors (arterial hypertension), are well known and our study corroborates these associations. Future prospective and longitudinal studies in both but separately type 1 and type 2 diabetes population, are needed to characterize others risk factors such as duration of disease or smoking which are involving in the development of ED. Furthermore, patients with erectile dysfunction are at an increased risk for cardiovascular morbidity and/or mortality as well as for all-cause death. Thus, clinicians should have in mind that screening of ED in diabetes patients is a part of the assessment of their cardiovascular risk.

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Table 1-Meta-analysis results of prevalence of erectile dysfunction in people with diabetes

Outcome	Number of study estimates	Number of participants	Prevalence (%)	95% CI		Between group p value	I^2 (%)
ED (main analysis)	**145**	**88,577**	**59.1**	**55.5**	**62.7**	**-**	**99**
Continent						*<0.0001*	
Africa	*15*	*2,055*	***71.3***	*63.2*	*78.2*		*92*
Asia	*61*	*36,032*	***67.0***	*60.4*	*73.1*		*99*
Europe	*48*	*3,7300*	***53.6***	*48.7*	*58.3*		*99*
North America	*17*	*10,509*	***34.5***	*26.1*	*44.0*		*99*
South America	*1*	*114*	***74.6***	*65.8*	*81.7*		*-*
Oceania	*1*	*788*	***74.4***	*71.2*	*77.3*		*-*
Multi-continent	*2*	*1,779*	***39.7***	*37.5*	*42.0*		*0*
Type of diabetes						*<0.0001*	
Type 1	*12*	*5,604*	***37.5***	*30.8*	*44.6*		*96*
Type 2	*70*	*44,488*	***66.3***	*61.5*	*70.9*		*99*
Both	*18*	*20,061*	***57.7***	*47.6*	*67.2*		*99*
Not declared	*45*	*18,424*	***53.9***	*45.6*	*62.0*		*99*
Setting						*0.37*	
Community	9	*3,163*	***66.9***	*52.5*	*78.7*		*98*
Outpatients	131	*84,225*	***58.8***	*54.9*	*62.7*		*99*
Not declared	5	*1,189*	***52.8***	*39.0*	*66.2*		*94*
Type of article						*0.79*	
Original article	114	*72,371*	***59.4***	*55.2*	*63.5*		*99*
Conference abstract	31	*16,206*	***58.2***	*50.2*	*65.8*		*99*
Diagnosis of ED						*<0.0001*	
IIEF-5	90	*41,025*	***60.7***	*55.9*	*65.3*		*99*

	SHIM	17	*7,093*	***82.2***	*74.8*	*87.7*		*99*
	Other	38	*40,459*	***42.3***	*37.1*	*47.7*		*99*
Mean age							*0.03*	
	18-60 years	55	*21,220*	***62.2***	*56.1*	*67.9*		*99*
	≥60 years	*23*	*10,432*	***66.7***	*57.5*	*74.8*		*99*
	Not declared	67	*56,925*	***53.8***	*48.3*	*59.3*		*99*

Abbreviations:

Table 2. Meta regression of continuous moderators of erectile dysfunction presence in people with diabetes.

Moderator*	Number of comparisons	β	95% CI		P-value	R^2
Duration of diabetes (years)	46	-0.02	-0.05	0.00	0.08	0.06
Percentage of people with neuropathy	32	0.02	-0.00	0.04	0.08	0.00
Percentage of people with retinopathy	30	0.004	-0.01	0.02	0.66	0.00
Percentage of people with cardiovascular disease	38	-0.005	-0.03	0.01	0.56	0.00
Percentage of people with kidney failure	22	0.02	-0.005	0.05	0.11	0.05
Mean body mass index	31	0.06	-0.06	0.18	0.30	0.00
Percentage of actual smokers	49	-0.007	-0.03	0.007	0.33	0.00
Percentage of people with hypertension	**50**	**0.03**	**0.008**	**0.04**	**0.003**	**0.00**

Abbreviations:

Figure 1. PRISMA flow-chart

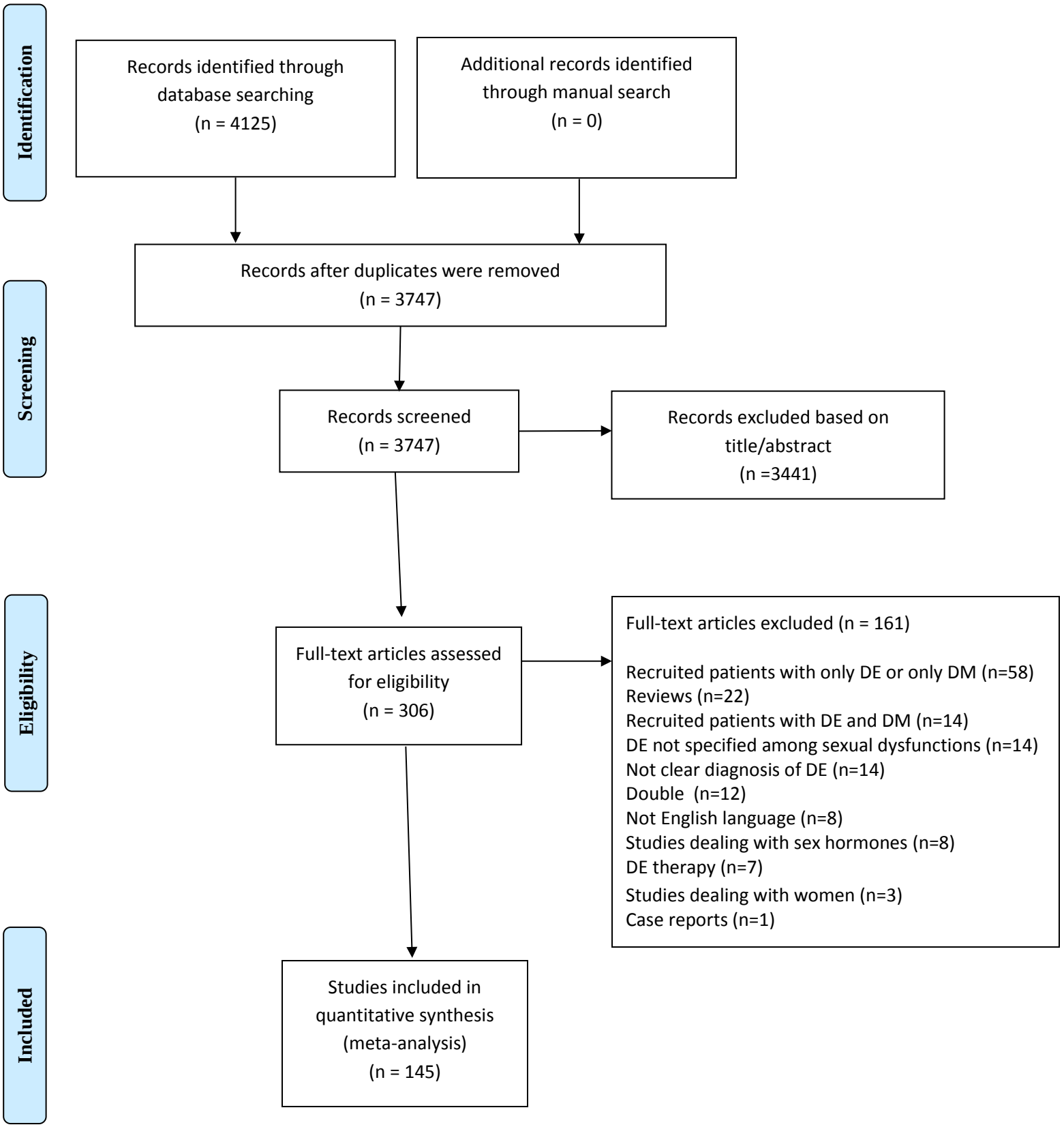
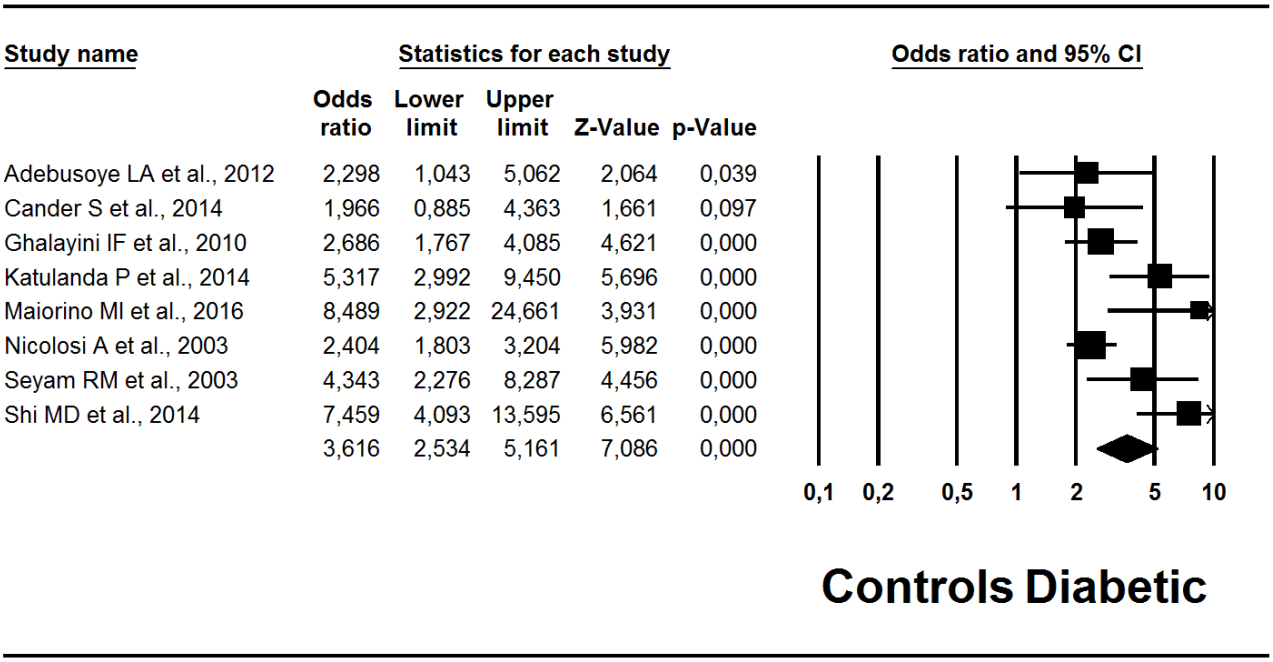


Figure 2. Prevalence of erectile dysfunction in diabetic and control subjects.



Supplementary Table 1. Descriptive characteristics of the studies included.

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Ab Rahman AA et al., 2011	544	Malaysia	Not available	Outpatients	IIEF-5
Adebusoye LA et al., 2012	33	Nigeria	Not available	Outpatients	IIEF-5
Adegite A et al., 2009	66	Nigeria	Type 2	Outpatients	IIEF-5
Ahmad S et al., 2010	281	Malaysia	Not available	Outpatients	IIEF-5
Ahmed A et al., 2011	333	Quatar	Not available	Outpatients	SHIM
Ahmed I et al., 2013	217	Pakistan	Type 2	Outpatients	SHIM
Ahn TY et al., 2007	127	Korea	Not available	Community	IIEF-5
Al Naimi A et al., 2014	209	Quatar	Not available	Outpatients	IIEF-5
Al-Hunayan A et al., 2007	323	Kuwait	Type 2	Outpatients	IIEF-5
AlMogbel TA., 2014	376	Saudi Arabia	Type 2	Outpatients	IIEF-5
Al-Turki YA., 2007	186	Saudi Arabia	Both	Outpatients	Other
Ashok Shenoy K et al., 2012	50	India	Type 2	Outpatients	Other
Awad H et al., 2010	100	Egypt	Type 2	Outpatients	IIEF-5
Bacon CG et al., 2002	2108	USA	Both	Outpatients	Other
Batty GD et al., 2010	6304	United Kingdom	Type 2	Outpatients	Other
Berrada S et al., 2003	34	Marocco	Not available	Community	Other
Bjerggaard M et al., 2015	481	Denmark	Not available	Outpatients	IIEF-5
Blans MCA	90	Netherlands	Both	Outpatients	IIEF-5
Blumentals WA et al., 2003	3160	United Kingdom	Not available	Outpatients	Other
Boyd MJ et al., 2009	180	United Kingdom	Type 2	Outpatients	Other
Brooke JC et al., 2011	356	United Kingdom	Not available	Not available	IIEF-5
Cander S et al., 2014	68	Turkey	Type 2	Outpatients	IIEF-5
Caretta N et al., 2016	92	Italy	Type 2	Outpatients	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Cavan DA et al., 1987	292	Scotland	Not available	Outpatients	Other
Chakraborty K et al., 2013	84	India	Not available	Outpatients	IIEF-5
Chaudhary RK et al., 2016	175	China	Type 2	Outpatients	IIEF-5
Chew SK et al., 2013	324	Singapore	Type 2	Outpatients	Other
Chew SKH et al., 2013	289	Singapore	Type 2	Outpatients	Other
Cho NH et al., 2006	1312	Korea	Type 2	Outpatients	IIEF-5
Chuang YC et al. 2012	455	China	Type 2	Outpatients	SHIM
Cleveringa FGW et al., 2009	1611	Netherlands	Type 2	Outpatients	Other
Corona G et al., 2014	1503	Italy	Type 2	Outpatients	IIEF-5
Dan A et al., 2014	113	India	Both	Outpatients	IIEF-5
De Berardis G et al., 2003	1460	Italy	Type 2	Outpatients	Other
De Berardis G et al., 2007	670	Italy	Type 2	Outpatients	Other
Derosa G et al., 2012	88	Italy	Type 2	Outpatients	IIEF-5
Derosa G et al., 2015	206	Italy	Type 2	Outpatients	IIEF-5
Eardley I et al., 2007	1556	Multicountry	Not available	Community	Other
El Saghier EOA et al., 2015	70	Egypt	Type 2	Outpatients	IIEF-5
Elbendary MA et al., 2009	38	Egypt	Not available	Outpatients	IIEF-5
Fedele D et al., 2000	9756	Italy	Both	Outpatients	Other
Feldman HA et al., 1994	120	USA	Not available	Outpatients	IIEF-5
Fukui M et al., 2011	197	Japan	Type 2	Outpatients	IIEF-5
Furukawa S et al. 2016	332	Japan	Type 2	Outpatients	SHIM
Furukawa S et al., 2016	340	Japan	Type 2	Outpatients	SHIM
Garcia-Malpartida K et al., 2011	154	Spain	Type 2	Outpatients	IIEF-5
Gazzaruso C et al., 2004	260	Italy	Type 2	Outpatients	IIEF-5
Gazzaruso C et al., 2011	293	Italy	Type 2	Outpatients	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Georgescu O et al., 2010	292	Romania	Not available	Outpatients	IIEF-5
Georgescu O et al., 2013	292	Romania	Both	Outpatients	IIEF-5
Ghalayini IF et al., 2010	118	Jordan	Not available	Community	IIEF-5
Ghazi S et al., 2012	391	Egypt	Type 2	Outpatients	IIEF-5
Ghenciu V et al., 2012	45	Moldavia	Type 2	Not available	Other
Giorda CB et al., 2013	1503	Italy	Type 2	Outpatients	Other
Giugliano F et al., 2010	555	Italy	Type 2	Outpatients	IIEF-5
Giuliano FA et al., 2004	2377	France	Both	Outpatients	IIEF-5
Goyal A et al., 2013	348	India	Not available	Outpatients	IIEF-5
Habibi A et al., 2011	171	Iram	Type 2	Outpatients	IIEF-5
Habibi A, 2010	171	Iram	Not available	Outpatients	IIEF-5
Hackett G et al., 2013	190	United Kingdom	Type 2	Outpatients	IIEF-5
Hackett GI et al., 2009	415	United Kingdom	Type 2	Outpatients	SHIM
Hamilton EJ et al., 2016	788	Australia	Type 2	Community	SHIM
Hassan A et al., 2014	429	Saudi Arabia	Type 2	Outpatients	ADAM
Henis O et al., 2011	102	Israel	Type 2	Outpatients	SHIM
Hermans MP et al., 2009	221	Belgium	Type 2	Outpatients	IIEF-5
Hopcan MB et al., 2010	372	Turkey	Not available	Outpatients	IIEF-5
Hotaling J et al., 2010	528	USA	Not available	Outpatients	IIEF-5
Hotaling JM et al., 2012	528	USA	Type 1	Outpatients	IIEF-5
Idung AU et al., 2012	86	Nigeria	Not available	Outpatients	IIEF-5
Jacobson AM et al., 2013	664	USA	Type 1	Outpatients	IIEF-5
Jacobson AM et al., 2015	644	USA	Type 1	Outpatients	IIEF-5
Jamieson F et al., 2008	142	United Kingdom	Type 1	Outpatients	Other
Jayanthy R et al., 2014	60	India	Not available	Not available	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Jayawardena RM et al., 2013	536	Sri Lanka	Not available	Outpatients	IIEF-5
Jiann BP et al., 2009	844	Taiwan	Type 2	Outpatients	SHIM
Justo D et al., 2010	103	Israel	Not available	Outpatients	SHIM
Kalter-Leibovici O et al., 2005	1040	Israel	Both	Outpatients	IIEF-5
Kamenov ZA et al., 2007	150	Bulgaria	Both	Outpatients	Other
Kapoor D et al., 2007	198	United Kingdom	Type 2	Outpatients	ADAM
Katulanda P et al., 2014	125	Sri Lanka	Not available	Outpatients	Other
Kempa T et al., 2015	150	South Africa	Both	Community	SHIM
Khatib FA et al., 2006	988	Jordan	Not available	Outpatients	IIEF-5
Klein R et al., 1996	359	USA	Not available	Outpatients	Other
La Vignera S et al., 2009	110	Italy	Not available	Outpatients	IIEF-5
Liu HY et al. 2016	785	China	Type 2	Outpatients	SHIM
Liu RT et al., 2012	453	China	Type 2	Outpatients	SHIM
Lo WH et al., 2014	603	China	Type 2	Outpatients	IIEF-5
Lu CC et al., 2009	792	Taiwan	Type 2	Outpatients	SHIM
Ma RCW et al., 2008	2306	China	Type 2	Outpatients	Other
Maiorino MI et al., 2015	118	Italy	Type 1	Outpatients	IIEF-5
Maiorino MI et al., 2016	151	Italy	Type 1	Outpatients	IIEF-5
Majzoub A et al., 2015	1052	Quatar	Not available	Outpatients	IIEF-5
Malavige LS et al., 2008	253	Sri Lanka	Type 2	Outpatients	IIEF-5
Malavige LS et al., 2015	232	United Kingdom	Not available	Outpatients	IIEF-5
Malavige LS., 2010	232	United Kingdom	Not available	Outpatients	IIEF-5
Mansour A.A.	2414	Iraq	Type 2	Outpatients	Other
McCulloch DK et al., 1980	541	Germany	Not available	Outpatients	Other
Meena BL et al., 2009	50	India	Type 2	Outpatients	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Mehtiyev TV, 2015	261	Azerbaijan	Type 2	Outpatients	IIEF-5
Meo SA et al., 2011	2250	Saudi Arabia	Not available	Outpatients	IIEF-5
Miccoli R et al., 1985	77	Italy	Not available	Outpatients	Other
Miccoli R et al., 1987	128	USA	Not available	Outpatients	Other
Mofid A et al., 2009	700	Iran	Both	Outpatients	Other
Mota M et al., 2003	310	Romania	Not available	Outpatients	SHIM
Mutagaywa RK et al., 2014	312	Tanzania	Both	Outpatients	IIEF-5
Nakanishi S et al., 2004	112	Japan	Type 2	Outpatients	Other
Nam SM et al., 2010	300	Korea	Type 2	Outpatients	IIEF-5
Nasser J et al., 2015	415	Bahrain	Type 2	Outpatients	IIEF-5
Nicolosi A et al., 2003	223	Multicountry	Not available	Community	Other
Olarinoye JK et al., 2006	77	Nigeria	Type 2	Outpatients	IIEF-5
Owiredu WKBA et al., 2011	274	Ghana	Not available	Outpatients	GRISS
Penson DF et al., 2009	571	USA	Type 1	Outpatients	IIEF-5
Pop-Busui R et al., 2013	644	USA	Type 1	Outpatients	IIEF-5
Pop-Busui R et al., 2014	635	USA	Type 1	Not available	IIEF-5
Pop-Busui R et al., 2015	635	USA	Type 1	Outpatients	IIEF-5
Rombopoulos G et al., 2009	400	Greece	Not available	Outpatients	IIEF-5
Rosen RC et al., 2009	373	USA	Type 2	Outpatients	IIEF-5
Rozhivanov RV et al., 2006	611	Bulgaria	Both	Outpatients	Other
Rutte A et al., 2015	108	Netherlands	Type 2	Outpatients	IIEF-5
Rutte A et al., 2015	154	Netherlands	Type 2	Outpatients	BSSC-M
Sampanis C et al., 2012	93	Greece	Type 2	Not available	IIEF-5
Schaan BD et al., 2013	114	Brazil	Type 2	Outpatients	IIEF-5
Selim S et al., 2015	3790	Bangladesh	Type 2	Outpatients	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Seyam RM et al., 2003	40	Egypt	Not available	Community	Other
Seyoum B., 1998	292	Ethiopia	Both	Outpatients	Other
Shabsigh R et al., 2010	234	USA	Not available	Outpatients	IIEF-5
Shankar A et al., 2013	582	India	Type 2	Outpatients	SHIM
Shi MD et al., 2014	105	Taiwan	Type 2	Outpatients	IIEF-5
Song HJ et al., 2013	124	Korea	Type 2	Outpatients	IIEF-5
Sonomtseren S et al., 2009	146	Mongolia	Type 2	Outpatients	IIEF-5
Taloyan M et al., 2012	190	Sweden	Type 2	Outpatients	Other
Tisdall AR et al., 2009	70	Ireland	Not available	Outpatients	IIEF-5
Turek SJ et al., 2013	301	USA	Type 1	Outpatients	IIEF-5
Vaswani A.S et al., 2011	390	Pakistan	Not available	Outpatients	IIEF-5
Viswanathan V et al., 2009	423	India	Type 2	Outpatients	IIEF-5
Wang CC et al., 2010	226	Taiwan	Type 2	Outpatients	IIEF-5
Wang F et al., 2013	1466	Canada	Both	Outpatients	Other
Webb EM et al., 2015	92	South Africa	Both	Outpatients	SHIM
Wessells H et al., 2011	571	USA	Type 1	Outpatients	IIEF-5
Wu C et al., 2012	127	China	Not available	Community	IIEF-5
Yamasaki H et al., 2004	82	Japan	Type 2	Outpatients	IIEF-5
Yang G et al., 2010	5477	China	Type 2	Outpatients	IIEF-5
Yildiz H et al., 2015	127	Turkey	Both	Outpatients	IIEF-5
Yu LW et al., 2010	313	China	Type 2	Outpatients	IIEF-5
Ziaei-Rad M et al., 2010	199	Iran	Both	Outpatients	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Total	**88,577**		**Type 1: 12; type 2: 70; both: 18; not declared: 45**	**Outpatients: 131; community: 9; not declared: 5**	**IIEF-5: 90; SHIM: 17; others: 38**

Abbreviations:

Supplementary Table 2. References of the studies included in the meta-analysis.

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